

Oxytetracycline-Injectable Clinical Field Trials - INAD 9027

1998 Annual Summary Report on the Use of Oxytetracycline-Injectable in Field Efficacy Trials

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Summary

Oxytetracycline as an injectable was used at only one U.S. Fish and Wildlife Service hatchery during 1998 to evaluate its effectiveness to prevent pre- and/or post-spawning mortality in paddlefish and pallid sturgeon broodstocks caused by systemic bacterial infection. The U.S. Food and Drug Administration has authorized the use of this compound under the Compassionate Investigational New Animal Drug Exemption #9027 for the purpose of collecting pivotal and ancillary efficacy data to support a new animal drug approval for oxytetracycline. Oxytetracycline as an injectable was administered in 2 trials and involved a total of 59 fish. Treatment in both trials appeared efficacious as post-spawning mortality was lower than observed during previous years efforts to spawn these species in which oxytetracycline injection treatment was not administered.

Introduction

In warmwater fish culture, oxytetracycline has been found to be efficacious for the control of bacterial hemorrhagic septicemia, pseudomonas disease, and enteric septicemia of catfish caused by *Edwardsiella ictaluri*. Fish culturists have also reported oxytetracycline to be effective against flexibacteriosis in catfish, sturgeon, paddlefish, temperate basses, sunfishes, and other fish species.

Although integrated fish health management practices are often successful in preventing the occurrence of the above-described diseases, adverse environmental conditions, fish handling procedures, physiological changes related to the onset and completion of spawning, and other culture related factors can lead to severe disease outbreaks requiring prompt treatment. An injectable drug product can effectively prevent losses in broodstock and other valuable non-feeding fish. Such treatment also reduces the discharge of infectious agents into the environment, thereby reducing the spread of disease to both cultured and wild fish.

Treatment strategies for the use of oxytetracycline as an injectable have been designed primarily to prevent or control pre- and post-spawning mortality in valuable broodstock populations. The overall objective of these studies was to minimize the impact of disease on fish health, fish quality, and survival in order to fully meet fishery management objectives. As many factors can affect the success or failure of oxytetracycline therapy, data were collected on a variety of parameters to help determine appropriate use patterns for oxytetracycline under routine fish culture conditions. These data should provide valuable information with respect to potential oxytetracycline use patterns in aquaculture.

Purpose

The primary purpose of this report is to summarize the results of calendar year 1998 (CY 98) supplemental oxytetracycline as an injectable (OTI) field efficacy studies. However, it is also expected that data from these studies will be used to enhance the existing OTI database that has been established from previous years studies for the purpose of expanding and/or extending the approved label for oxytetracycline use in aquaculture.

Facilities, Materials, and Methods

1. Facilities

Only a single U.S. Fish and Wildlife Service National Fish Hatchery (Natchitoches NFH) used OTI during CY 98.

2. OTI used in trials

All OTI used in these trials was Liquamycin LA-200 supplied by Pfizer, Inc., Lee's Summit, Missouri. Pfizer's over-the-counter injectable Liquamycin LA-200 contains 200 mg of active oxytetracycline amphoteric per milliliter, and 1.8% magnesium oxide. Pfizer's Liquamycin LA-200 was the only form of injectable oxytetracycline used to treat fish under INAD #9027.

3. Drug dosages

As described in the Study Protocol for INAD #9027, Investigators were allowed to use OTI as either a single injection treatment at the standard terrestrial animal dosage of 20 mg of active oxytetracycline per kg of fish body weight; or at various dosages and multiple treatment frequencies. If used as a single injection at 20 mg/kg body weight, a 30 d withdrawal period was required. All other treatment regimes required a 60 d withdrawal period. Oxytetracycline dosages used in these studies included 25mg OTI/kg (paddlefish) and 100mg OTI/kg (pallid sturgeon).

Fish Species and Diseases Treated

1. Species of fish treated

Two fish species were treated during CY 98. Species treated included paddlefish (*Polydon spathula*) and pallid sturgeon (*Scaphirhynchus albus*).

2. Diseases treated

All fish were treated prophylactically to prevent potential bacterial infection. Paddlefish and pallid sturgeon broodstocks have both been shown to be susceptible to bacterial infection prior to, during, and following spawning.

Data Collected

1. Pathologist's reports

Fish health pathology reports provide essential information with respect disease confirmation. However, no pathologist reports were submitted during CY 98 studies.

2. Mortality data

As stated in the Study Protocol, mortality data was to be collected for at least 10 days prior to treatment, during the treatment period, and for at least 30 days post-treatment. Investigators were strongly encouraged to collect mortality data on a daily basis. However, in these trials daily collection of mortality data was not always possible as fish were being held in ponds. Therefore, mortalities were collected, counted, and recorded on an intermittent basis throughout the entire study period.

Discussion of 1998 Study Results:

1. Summary results on the efficacy of OTI for the control of bacterial diseases in non-salmonid fish

A. Efficacy at 25 mg/kg body weight

OTI was used at 25 mg/kg body weight in a single trial involving paddlefish. Thirty-six fish were injected a single time immediately following completion of spawning. All females were spawned by caesarian section, which is a quite invasive procedure and can often lead to resultant bacterial infection. Although 6 of 36 treated fish (~17%) died during the post-spawn recovery period, all mortalities were attributed to spawning-related stresses. Based on previous experience by staff at this facility with respect to the spawning and holding of

adult paddlefish, OTI treatment was considered to be efficacious (Table 1).

B. Efficacy at 100 mg/kg body weight

OTI was used at 100 mg/kg body weight in a single trial involving pallid sturgeon. Twenty-three fish were injected 1-3 times on between 1/20/98 and 6/8/98. Fish were injected immediately following pre-spawning biopsy procedures, following spawning procedures, and/or prior to release (note: pallid sturgeon are a Threatened/Endangered species and no harvest is allowed). All females were spawned by caesarian section, an invasive procedure that can often lead to resultant bacterial infection. No mortalities were reported. Based on previous experience by staff at this facility with respect to the spawning and holding of pallid sturgeon, OTI treatment appeared to be efficacious (Table 1).

2. Observed Toxicity

No toxicity or adverse effects relating to OTI treatment were reported.

Summary of Study Results

Oxytetracycline as an injectable was used at dosages of 25 and 100 mg/kg body weight. Treatment was administered as a single injection (25 mg/kg), or as multiple injections (100 mg/kg; 1-3- times). Trials involved the prophylactic treatment of paddlefish and pallid sturgeon broodstocks at a single facility. A total of 59 adult fish were treated. Water temperature during the treatment of all fish was 18.3°C. Both trials conducted in CY 98 appeared to be efficacious. Determination of efficacy was based primarily on previous years' experience at the hatchery indicating significant post-spawning mortality of untreated fish. Furthermore, Investigators reported no evidence of toxicity of adverse effects related to OTI treatment. However, based on a lack of untreated control fish, replication, randomization, etc., it is understood that these data can only be considered as ancillary data. None-the-less, the ancillary data described above should provide useful corroborative data to support a future expanded label claim for oxytetracycline. It is anticipated that additional ancillary efficacy data will continue to be collected under INAD #9027. In future trials conducted under INAD 9027, efforts will be directed towards the generation of higher quality data.

Table 1. Summary of 1998 Oxytetracycline-Injectable Efficacy Results

Hatchery	Number of Trials	Fish Species	Number of Fish	Treatment type	Number of treatments	Dose (mg/kg bw)	Temp. (°C)
Natchitoches NFH	1	PAH	36	Prophylactic	1	25	18.33
	1	PLS	23	Prophylactic	1-3	100	18.33

Table 2. Summary Data Regarding 1998 Oxytetracycline as an Injectable Efficacy Studies

Total Number of Fish Treated:	59
Treatment Regimes Used:	
25 mg/kg body weight (1 time)	1 trial
100 mg/kg body weight (1-3 times)	1 trial
Treatment Water Temperature (°C):	18.3
Size of Treated Fish:	Adult
Species Treated:	paddlefish (<i>Polydon spathula</i>) pallid sturgeon (<i>Scaphirhynchus albus</i>)
